Complete Summary

GUIDELINE TITLE

ASHP therapeutic guidelines on the pharmacologic management of nausea and vomiting in adult and pediatric patients receiving chemotherapy or radiation therapy or undergoing surgery.

BIBLIOGRAPHIC SOURCE(S)

American Society of Health System Pharmacists (ASHP). ASHP therapeutic guidelines on the pharmacologic management of nausea and vomiting in adult and pediatric patients receiving chemotherapy or radiation therapy or undergoing surgery. Am J Health Syst Pharm 1999 Apr 15;56(8):729-64. [423 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Nausea and vomiting induced by chemotherapeutic agents, radiation therapy, or surgery

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness

CLINICAL SPECIALTY

Anesthesiology
Nutrition
Oncology
Surgery

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Nurses
Pharmacists
Physicians

GUIDELINE OBJECTIVE(S)

To assist health care professionals in the appropriate management of adult and pediatric patients, in both inpatient and outpatient settings, with nausea and vomiting induced by chemotherapeutic agents, radiation therapy, or surgery

TARGET POPULATION

Adults and children with nausea and vomiting, actual or anticipated, induced by chemotherapeutic agents, radiation therapy, or surgery

INTERVENTIONS AND PRACTICES CONSIDERED

1. Factors effecting the potential for emesis with chemotherapeutic agents, radiation or surgery
2. Prevention and treatment of breakthrough chemotherapy-induced nausea and vomiting
3. Prevention of delayed chemotherapy-induced emesis
4. Prevention and treatment of radiation therapy-induced nausea and vomiting
5. Prevention and treatment of postoperative nausea and vomiting
6. Managing patients who are unresponsive to prophylactic antiemetic therapy

MAJOR OUTCOMES CONSIDERED

Primary clinical endpoint, Complete response: the number of patients with no vomiting episodes

Secondary endpoints:

- The number of patients with no nausea or retching
- Frequency of emetic episodes
- Severity of nausea

Humanistic outcomes [quality of life assessment with the Functional Living Index-Cancer (FLIC) and the Functional Living Index-Emesis (FLIE) instruments or the health-related quality of life questionnaire])

Economic outcomes (i.e., length of hospital stay)

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

A comprehensive literature search was performed. Published studies identified through a MEDLINE search (1966 to April 1998) were reviewed, as were the reference lists of the retrieved documents and abstracts from meetings of professional associations, when appropriate.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The literature was critically evaluated, including examination of research design, patient selection, medication dose, route, combination treatment, test measures, statistics, and results.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The American Society of Health-System Pharmacists (ASHP) Therapeutic Guidelines on the Pharmacologic Management of Nausea and Vomiting in Adult and Pediatric Patients Receiving Chemotherapy or Radiation Therapy or Undergoing Surgery were prepared by the University of Kentucky Drug Information Center under contract to ASHP. The project was coordinated by the director of the center, who worked in conjunction with an independent panel of seven clinical specialists (a physician, a nurse, and five pharmacists) representing adult and pediatric hematology–oncology and surgery–anesthesia. The panel was appointed by ASHP and was created to ensure that applicable studies were

included in the analysis, to provide expert judgment when the literature was of poor quality or lacking, and to provide insight into the clarity, practicality, and flexibility of the document in clinical practice.

The guidelines were circulated in draft form, and all members of the panel had the opportunity to comment on the recommendations and strengths of evidence.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Recommendations were graded A, B, C or D according to the strength of scientific evidence:

A. Strong research-based evidence (multiple relevant and high-quality scientific studies)
B. Moderate research-based evidence (one relevant, high-quality scientific study or multiple adequate scientific studies)
C. Limited research-based evidence (at least one adequate scientific study in patients with nausea and vomiting, published in a reputable medical journal)
D. Panel interpretation of information that did not meet inclusion criteria as research-based evidence.

COST ANALYSIS

Published analyses on the cost-effectiveness of antiemetic agents were reviewed. From pharmacoeconomic studies it appears that 5-HT_3 receptor antagonists are a cost-effective choice for adults and children receiving moderately to highly emetogenic agents.

For a complete description of the reviewed studies, see the original guideline document.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guidelines underwent multidisciplinary field review to evaluate their validity, reliability, and utility in clinical practice. The final document was approved by the ASHP Commission on Therapeutics and the ASHP Board of Directors.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Prevention of chemotherapy-induced nausea and vomiting

Recommendation 1. The emetic potential of the chemotherapeutic agent (Table 3) is the primary factor to consider when deciding whether to administer

pharmacologic prophylaxis and which antiemetic(s) to select. (Strength of evidence = A)

Recommendation 2. Adult and pediatric patients receiving chemotherapeutic agent(s) with emetic potential classified as level 2 through 5 should receive pharmacologic prophylaxis against nausea and vomiting each day on which chemotherapy is given. (Strength of evidence = B) Antiemetic prophylaxis is not required when the level of emetogenicity is 1.

a. Adult and pediatric patients receiving level-2 chemotherapeutic regimens can receive dexamethasone or methylprednisolone alone for prophylaxis of nausea and vomiting. (Strength of evidence = B) Prochlorperazine is also an option for adults. (Strength of evidence = D)
b. Adult and pediatric patients receiving chemotherapeutic agent(s) with emetic potential of level 3 through 5 should receive a corticosteroid (dexamethasone or methylprednisolone) in combination with a 5-HT_3 receptor antagonist. (Strength of evidence = A for adults and C for pediatric patients)
c. Orally and intravenously administered antiemetics are generally equivalent in efficacy and safety for both adult and pediatric patients. (Strength of evidence = B for adults and C for pediatric patients) The decision as to which formulation to use should be based on patient-specific factors and cost.
d. The decision as to which 5-HT_3 receptor antagonist to use should be based on the acquisition cost of comparable doses. (Strength of evidence = A) (Tables 6 and 7) Dosage recommendations for adult and pediatric patients differ.

Treatment of breakthrough chemotherapy-induced nausea and vomiting

Recommendation 3. All patients receiving chemotherapy should have antiemetics available on an as-needed basis for rescue for breakthrough nausea and vomiting. (Strength of evidence = A) Patients should be educated on the appropriate administration of and expectations for therapy and should be reassured that every effort is being made to prevent symptoms. In adults, lorazepam, methylprednisolone, prochlorperazine, metoclopramide, dexamethasone, haloperidol, and dronabinol are effective. (Strength of evidence = C) In pediatric patients, chlorpromazine, lorazepam, or methylprednisolone (or dexamethasone) is recommended. (Strength of evidence = B) The choice of agent should be based on patient-specific factors (e.g., anticipated adverse effects, past success) and cost.

Prevention of delayed chemotherapy-induced emesis

Recommendation 4. For the prevention of delayed emesis after cisplatin therapy in adults, dexamethasone with metoclopramide or a 5-HT_3 receptor antagonist is recommended. (Strength of evidence = A) The choice of agent should be based on patient-specific factors and cost. For delayed emesis after cyclophosphamide, doxorubicin, or carboplatin therapy, a 5-HT_3 receptor antagonist with dexamethasone is recommended. (Strength of evidence = B) Prochlorperazine in combination with dexamethasone has also been used and is available in extended-release and rectal dosage forms, but the evidence to support this combination is limited. (Strength of evidence = D) In pediatric patients, chlorpromazine, lorazepam, or a 5-HT_3 receptor antagonist can be used in combination with a corticosteroid. (Strength of evidence = C)

Prevention of radiation therapy-induced nausea and vomiting

Recommendation 5. Patients receiving total or hemibody irradiation (with or without concomitant chemotherapeutic agents) or single-exposure, high-dose radiation therapy to the upper abdomen should receive preventive therapy for nausea and vomiting with each day of therapy. (Strength of evidence = A) A 5-HT_3 receptor antagonist should be used both in adults and in pediatric patients. (Strength of evidence = B) Oral therapy should be encouraged; however, i.v. therapy is an acceptable option. (Strength of evidence = B) There is no evidence to support the use of 5-HT_3 receptor antagonists 24 hours beyond the last dose of radiation.

Treatment of radiation therapy-induced nausea and vomiting

Recommendation 6. If an agent is needed to treat established radiation therapy-induced emesis in adults, prochlorperazine, metoclopramide, or thiethylperazine is recommended. 5-HT_3 receptor antagonists are also an option. Chlorpromazine and lorazepam can be used in pediatric patients. (Strength of evidence = D)

Prevention of postoperative nausea and vomiting

Recommendation 7. Patients who are at high risk of vomiting should receive antiemetic prophylaxis against postoperative nausea and vomiting. (Strength of evidence = C)

Recommendation 8. When prophylaxis is indicated, droperidol or a 5-HT_3 receptor antagonist is recommended for the prevention of postoperative nausea and vomiting in adult and pediatric patients. (Strength of evidence = A) Other medications that have been studied extensively and that are considered to be alternatives include chlorpromazine, prochlorperazine, metoclopramide, and promethazine. (Strength of evidence = B) Because droperidol and 5-HT_3 receptor antagonists are effective, the choice of agent should be based on patient-specific factors and cost. Metoclopramide and prochlorperazine should generally not be used in pediatric patients. (Strength of evidence = C)

Treatment of postoperative nausea and vomiting

Recommendation 9. Droperidol or 5-HT_3 receptor antagonists are recommended for adult and pediatric patients with established postoperative nausea and vomiting. (Strength of evidence = A) Other medications that have been studied extensively and that are considered to be alternatives include chlorpromazine, prochlorperazine, and promethazine. (Strength of evidence = B) The choice of agent should be based on patient-specific factors and cost. Prochlorperazine and metoclopramide should generally not be used in pediatric patients.

Managing patients who are unresponsive to prophylactic antiemetic therapy

Recommendation 10. When patients do not respond to initial therapy with an antiemetic agent, it is recommended that an agent from another pharmacologic

class be added, that the dose of the antiemetic be increased to the maximum within an accepted range, or that a combination of both approaches be used. (Strength of evidence = D)

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (See "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate management of nausea and vomiting in adult and pediatric patients receiving chemotherapeutic agents or radiation therapy or undergoing surgery has the potential to substantially improve clinical, humanistic, and economic outcomes. These include reduction in the frequency, severity and duration of nausea and vomiting, and improved quality of life.

POTENTIAL HARMS

Adverse Effects of Antiemetic Agents

Medication	Adverse Effects*
Antihistamines • Diphenhydramine • Hydroxyzine	Most common: sedation, dry mouth, constipation; Less common: confusion, blurred vision, urinary retention
Belladonna alkaloid • Scopolamine	Most common: dry mouth, drowsiness, impaired eye accomodation; Rare: disorientation, memory disturbances, dizziness, hallucinations
Benzamide • Benzquinamide • Metoclopramide	Most common: sedation restlessness, diarrhea (metoclopramide), agitation, central nervous system depression Less common: extrapyramidal effects (more

• Trimethobenzamide	frequent with higher doses), hypotension, neuroleptic syndrome, supraventricular tachycardia (with i.v. administration)
Benzodiazepines	Most common: sedation, amnesia
• Lorazepam	Rare: respiratory depression, ataxia, blurred vision, hallucinations, paradoxical reactions (weeping, emotional reactions)
Butyrophenones	Most common: sedation, hypotension, tachycardia
• Droperidol • Haloperidol	Less common: extrapyramidal effects , dizziness, increase in blood pressure, chills, hallucinations
Cannabinoids	Most common: drowsiness, euphoria, somnolence, vasodilation, vision difficulties, abnormal thinking, dysphoria
• Dronabinol	Less common: diarrhea, flushing, tremor, myalgia
Corticosteroids	Most common: gastrointestinal upset, anxiety, insomnia
• Dexamethasone • Methylprednisolone	Less common: hyperglycemia, facial flushing, euphoria
Phenothiazines	Most common: sedation, lethargy, skin sensitization
• Prochlorperazine • Promethazine • Chlorpromazine • Triethylperazine	Less common: cardiovascular effects, extrapyramidal effects, cholestatic jaundice, hyperprolactinemia
	Rare: neuroleptic malignant syndrome, hematologic abnormalities
Serotonin Antagonists	Most common: headache, asymptomatic prolongation of electrocardiographic interval
• Ondansetron • Granisetron • Dolasetron	Less common: constipation, asthenia, somnolence, diarrhea, fever, tremor or twitching, ataxia, lightheadedness, dizziness, nervousness, thirst, muscle pain, warm or flushing sensation on i.v. administration
	Rare: transient elevations in serum

transaminases

Most common = > 10%; less common = 1-10%; rare = < 1%. Based on FDA-approved labeling and generalized to the drug class

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

The recommendations in this document may not be appropriate for use in all clinical situations. Decisions to follow these recommendations must be based on the professional judgment of the clinician, individual patient circumstances, and available resources.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1999

GUIDELINE DEVELOPER(S)

American Society of Health-System Pharmacists - Professional Association

SOURCE(S) OF FUNDING

American Society of Health-System Pharmacists (ASHP)

GUIDELINE COMMITTEE

- American Society of Health-System Pharmacists (ASHP) Commission on Therapeutics
- The University of Kentucky Drug Information Center under contract to ASHP

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Project Coordinator: Mary lea Gora-Harper, PharmD.

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ASHP Staff Liaison: Leslie Dotson Jaggers, PharmD, BCPS.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Panel members and contractors were required to disclose any possible conflicts of interest before appointment.

GUIDELINE STATUS

This is the current release of the guideline.

According to the guideline developers, these guidelines are scheduled for review and update in two to four years from the original release date (1999).

GUIDELINE AVAILABILITY

Electronic copies: Available from the American Society of Health-System Pharmacists (ASHP) Web site.

Print copies: Available from the American Society of Health-System Pharmacists, 7272 Wisconsin Avenue, Bethesda, MD 20814.

AVAILABILITY OF COMPANION DOCUMENTS

None available

NGC STATUS

This summary was completed by ECRI on September 10, 1999. It was verified by the guideline developer on October 1, 1999.

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